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ORIGINAL ARTICLE

Spectral power, source localization and microstates to quantify chronic deficits from 'mild' closed head injury: Correlation with classic neuropsychological tests

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Abstract

Primary objective: To explore the quantitative relationship between neuropsychological impairment and spectral QEEG power, source localization (s-LORETA) and microstate duration in patients who 'fail to adapt' years after mild closed head injury.
Methods and procedures: Differences in classic psychometric measures, QEEG measures, s-LORETA indicators and microstate durations were compared for three levels of neuropsychological impairment ∼(average) 6 years after injury.
Results: Patients who displayed the moderate-to-severe neuropsychological impairments typical of mild TBIs exhibited shorter microstates, less power within the alpha band and lower power within the theta and delta bands within caudal regions. There were conspicuous differences in the configurations of microstates, their source localizations and frequency bands.
Conclusions: The systematic relationship between neuropsychological impairment as inferred by classic psychometric measures that can require tens of hours to collect and modern configurational analyses of brain activity that require ∼30 minutes suggests that the latter might be useful in discerning the area of dysfunction and potential focus of treatment for patients with closed head injury years after the event.

Keywords

Microstate durations, neuropsychological test batteries, quantitative electroencephalogram, source localization (s-LORETA), traumatic brain injury

History

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Introduction

Closed head injury is associated with a rapid change in acceleration of pressures or force per unit area that distributes mechanical energy through the cerebral volume. Although the long-term effects of severe brain injuries are often evident by direct neurological and computerized imaging, the long-term consequences of mild traumatic brain injuries (mTBI), often described as 'mild' closed head or concussive injuries, are often ambiguous [1]. Until recently the primary method of inference required standardized scores from performance-based neuropsychological test batteries such as the Halstead-Reitan Impairment Index [2] or means of standardized scores from aggregates of performance-based tests whose integrity are strongly dependent upon a particular cerebral region. Quantitative electroencephalography (QEEG) and the source localization algorithms derived from these data, such as standardized low resolution electromagnetic tomography (s-LORETA), added an addition level of resolution.

Quantitative Electroencephalography (QEEG) has been shown to discern changes associated with the post-concussion syndrome and to predict the level of improvement 1 year later [3]. It can distinguish normal patients from those with mild traumatic brain injury [4] and the later from more severe forms [5]. Recently, Naunheim et al. [6] developed a QEEG algorithm for inference of brain injury for an Emergency Department setting that revealed 90% specificity.

The changes in pattern, localization and amplitude within different frequency bands after a closed head injury are time-dependent. Shortly after the impact there are usually reductions in power within alpha frequency, but increased theta and delta power. Within the alpha range the power within 8–10 Hz increases, while the faster alpha interval decreases. Some variation of this pattern can be maintained for weeks to months. Thatcher et al. [7] reported that increased frontal and temporal coherence with less temporal difference between the two regions, increased differences in rostral-caudal amplitudes and reduced posterior power allowed moderately accurate classification of individuals with mild TBI compared to controls. This configuration was relatively stable 6 months after the injuries.

Classic neuropsychological test batteries often reveal standardized quantitative deficits whose profiles are commensurate with the reported or observed behavioural alterations subsequent to mild TBI. In a series of validation analyses for various test batteries for patients with mild TBI, Persinger and colleagues [8–10] found that the amount of

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z-score discrepancy between standardized scores for a composite of intelligence and memory and the aggregate score for neuropsychological tests was strongly related (phi = 0.85) to inferred brain damage. Repeated assessments 1 year and 2 years after a mild TBI indicated no significant change in several indices of neuropsychological impairment [8]. A non-linear relationship between severity of impairment and scores for the Depression scale from the Minnesota Multiphasic Personality Inventory [12] and the complex partial epileptic-like experiences profile [13] indicated that patients with mild TBI displayed the most extreme scores.

Although the general consensus has been that mild TBI is associated with short-term cognitive deficits that resolve within ~3 months after the injury, the assumption may not be accurate. About 15% of this population develops a post-concussion syndrome that can be incapacitating for years [14]. Many of these patients report complex partial epileptic-like experiences, but without classic or overt electroencephalographic correlates [15]. The convergence of information regarding the results from traditional neuropsychological assessments that require tens of hours to administer and QEEG profiles that require less than an hour to obtain would facilitate cross-validity and potentially alter methods of assessment for patients who, despite the 'mild' nature of the initial injury, cannot adapt to the pre-morbid vocational or familial demands. It was reasoned that discerning the quantitative relations between neuropsychological impairment and measures from the most modern QEEG technology and applications would yield valuable information. It was also assumed that if the effects were to be clinically useful, they should be clearly evident and reliable and internally consistent within a small population of patients.

Methods

Subjects

The database was created by extracting QEEG data and neuropsychological data from every patient ($n = 26$) who had undergone full neuropsychological assessments over an ~3-year period (January 2010–April 2013). Their mean age was 40 years (SD = 16.3 years). The mean and standard deviation for the delays between the mechanical impacts to the skulls and the assessments were 5.6 and 5.2 years, respectively (range = 0.3–16 years). All of them had been referred by external agencies for a full neuropsychological assessment to discern the level of functioning following a closed head injury due to an impact of concussive force or mechanical energies. They all met the criteria of mTBI on the bases of either a GSC of >13 or a suspension of consciousness of less than 20 minutes. All patients were administered the standard battery of intellectual, memory, academic achievement, classic (Halstead-Reitan Battery) and novel (e.g. Conditioned Spatial Association Test) neuropsychological, personality and quantitative electroencephalographic measurements [15]. On the basis of the Russell et al. [16] ordinal categories (in parentheses), subjects were assigned to one of three groups: no impairment (0 or 1), mild impairment (2) and moderate-to-severe impairment (3–5). They were partitions of the original Halstead-Reitan Impairment Index between 0–1 such that 0–0.1 = 0, 0.2–0.3 = 1, 0.4–0.5 = 2, 0.6–0.7 = 3, 0.8–0.9 = 4 and 1.0 = 5. There were nine, eight and nine patients in each group, respectively.

Procedure

Each assessment required 2 full days. Testing occurred between 10–18 hours. The QEEG data were collected in the final hour of the first day and required 45 minutes. Descriptions of the tests employed have been published elsewhere [8–11]. During the QEEG the patient sat in a comfortable chair in a dimly lit acoustic chamber. The client was informed that the QEEG assessment was not the same as an EEG performed by a neurologist and was utilized to help validate the results of the standard psychometric tests. The patient could communicate at any time with the EEG technicians through a microphone and speaker system.

The first phase of the QEEG collection was an eyes-open baseline (10 minutes). The client was asked to pick a spot on the wall in front of them and focus on that spot. They were told they could blink as much as needed but to try and remain as still as possible throughout the duration of the testing. The patient was then asked to close the eyes and to relax; the lights were dimmed. After the eyes-closed portion the client was asked to keep the eyes closed and breathe deeply but very slowly for ~45 seconds. After the 45 seconds they were told they could relax, keeping the eyes closed. After 30 seconds of relaxation they were again asked to deep breathe for 45 seconds at a slightly increased pace and then they were asked to relax. Finally, they were asked to breathe deeply a third time, again at a slightly increased pace for 45 seconds before relaxing. The patient was then disconnected from the EEG and this concluded day 1 of testing.

Quantitative electroencephalographic equipment

Brain activity was measured by a Mitsar-201 portable QEEG system (Saint Petersburg, Russia) that was connected to a 19-channel electrode cap (Electrode-Cap International) that contained the 10–20 Standard Electrode Placement. Electrode site include Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, T6, O1 and O2 that were linked to the ears (A1 and A2) for monopolar recordings. Impedance of all channels was less than 10 kOhm. Data were acquired using WinEEG v2.84.44 software with a sampling rate of 250 Hz. A 50–70 Hz notch filter was used in the WinEEG software for all subjects in order to filter high frequency noise during recording. The EEG record was inspected for movement artifacts; the principal component analyses (PCA) method of artifact correction within WinEEG software was employed where appropriate.

Analyses of QEEG data

All QEEG data were analysed using three different methods; spectral power, standardized low resolution brain electromagnetic tomography (s-LORETA) and microstate analysis. Spectral analysis was computed utilizing WINEEG software and further statistical analysis was completed using SPSS software. Spectral analysis was performed on 30 seconds of artifact-free EEG recorded from the 19 channels during periods when the individuals were relaxing with their eyes closed.

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Source localization (s-LORETA)

Source localization analyses were completed by standardized low-resolution electromagnetic tomography or s-LORETA [17, 18]. The same 30-second sample that was used to compute the spectral power was used for source localization. All 84 regions of interest (ROI), 42 from each hemisphere, for each of the software's defined frequency bands [delta (1.5–4 Hz), theta (4–7.5 Hz), alpha-1 (7.5–10 Hz), alpha-2 (10–13 Hz), beta-1 (13–20 Hz), beta-2 (20–25 Hz), beta-3 (25–30 Hz) and gamma (30–40 Hz)] were computed. The analysis calculated the activation of a single voxel at ROI centroid. Results were then extracted and exported into SPSS for statistical analysis. Finally, the regions were then summed based on their location (rostral, caudal or limbic).

Microstate analyses

Koenig et al. [19] have demonstrated consistent microstates whose durations are ~80–120 milliseconds. These microstates have been defined as periods of quasi-stable topographical maps of the overall scalp's electric field [20]. This research has revealed that there are four major stable microstates maps that have been determined to account for close to 80% of the variance in voltage fluctuations. It has also been found that these four microstates are consistent across age groups with varying durations and proportions [19]. Based on this information it has been hypothesized that these microstates could reflect a type of information processing [20].

The microstates were computed from 40 seconds of artifact-corrected EEG records taken from the 19 channel EEG during the eyes-closed baseline. The epochs were analysed using the procedures outlined by Koenig et al. [19], except that all clients were analysed in one analysis and the data was then individually exported for statistical analysis. The characteristics of the cumulative microstates of all clients were mapped and the durations were then analysed with respect to impairment index. To discern if the *qualitative* configuration of the microstates differed between the patients who displayed no neuropsychological impairment and those that displayed moderate-to-severe impairment (mild TBI), averaged microstates for both populations were extracted separately.

Results

Distribution of neuropsychological impairment

The Halstead Impairment Index was employed as the reference inference for brain dysfunction or injury. The Impairment Index is derived from seven scores from the battery and ranges from 0–1 with intermittent decimals. In this study, the ranges were divided according to Russell et al. [16] into increments of no impairment (0,1), mild impairment (2) and moderate–severe impairment (3+). The proportion of the patients assessed that were included in each of these three groups were 35%, 30% and 35%, respectively, which also reflects the approximate proportion for the last ~800 patients assessed over the last 25 years.

Other global indicators

In both clinical practice and following experimental analyses it has been found that toe graphaesthesia, which involves activity within the medial prefrontal lobe according to SPECT analyses [21], also reflects general impairment when the medial surface is involved. There was a significant difference in toe Graphaesthesia errors as a function of the three groups of Halstead-Reitan defined impairments [$F_{(2,21)} = 5.00$, $p = 0.018$, $\text{eta}^2 = 0.34$]. Post-hoc analysis indicated that patients with the most severe neuropsychological impairment displayed more toe graphaethesia errors. The groups differences were still present when the data were analysed by the Kruskal-Wallis test ($\chi^2 = 6.74$, $p = 0.034$). The results are shown in Figure 1.

Personality and 'electrical lability' differences

The results from the 16PF indicated that individuals who displayed mild or greater neuropsychological impairment were intrinsically lower on the liveliness factor (Figure 2) than those who sustained an impact and displayed no neuropsychological impairment [$F_{(2,18)} = 5.71$, $p = 0.013$, $\text{eta}^2 = 0.42$].

Only one scale Pt, or psychasthenia, from the 10 clinical scales of the MMPI-168 displayed significant group differences. Individuals with a moderate–severe impairment scored

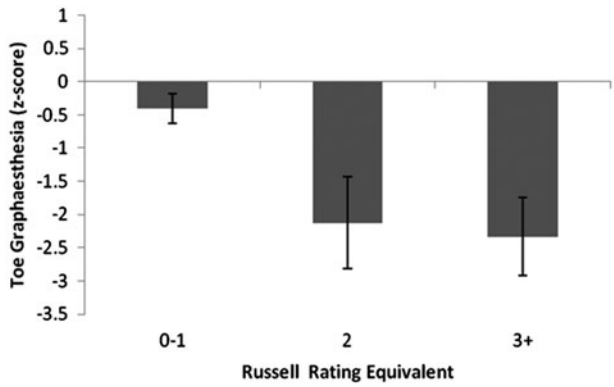

Figure 1. Standardized differences in scores for toe Graphaesthesia for groups with different levels of impairment. Vertical bars indicate SDs.

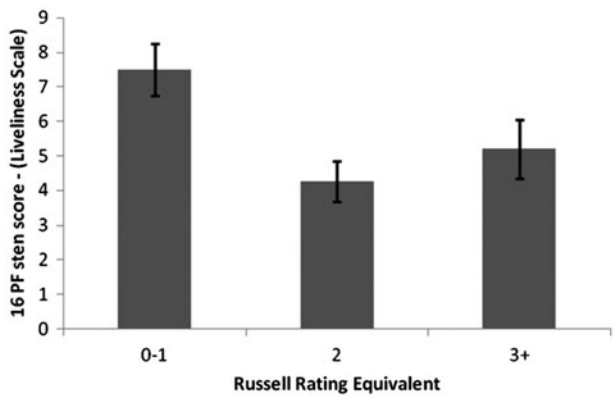

Figure 2. Sten scores for the 'lively' factor on the 16PF for groups with different degrees of neuropsychological impairment. Vertical bars indicate SDs.

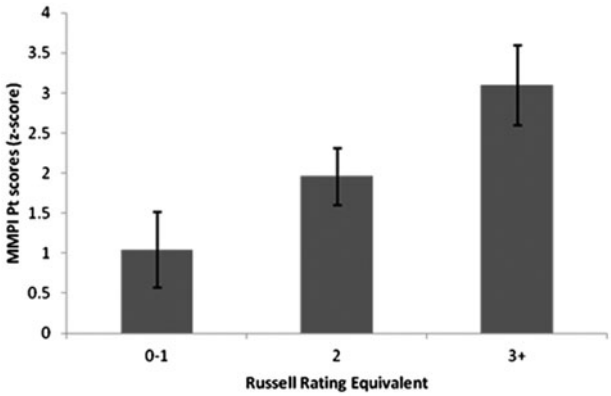

Figure 3. Means and standard deviations for the psychasthenia ('ruminative anxiety') scale of the MMPI for patients who displayed different severities of neuropsychological impairment.

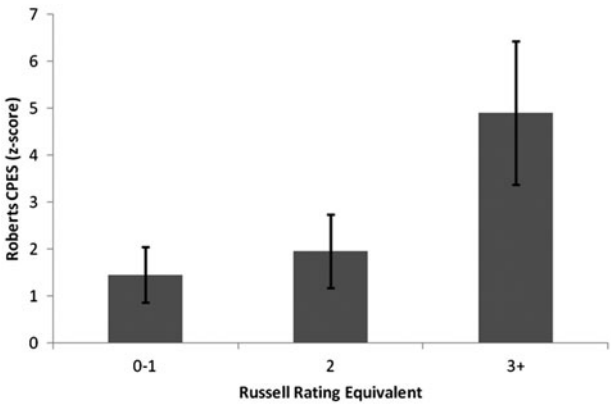

Figure 4. Means and standard deviations for the Roberts' Inventory for Complex Partial Epileptic Symptoms for patients whose impairment rating indicated no, mild or moderate-to-severe dysfunction.

significantly higher on this scale than those with no impairment [$F_{(2,21)} = 5.27$, $p = 0.015$, eta$^2 = 0.36$] (Figure 3). This result indicates that those individuals with a moderate–severe impairment have experienced significantly more worry, anxiety and tension than those with no impairment.

The Roberts et al. [22] CPES inventory assesses the temporal incidence of complex partial seizure-like symptoms and signs based upon subjective reports. The group who was measured to have moderate–severe impairment reported they experienced significantly elevated scores on this test [$F_{(2,20)} = 3.546$, $p = 0.050$, eta$^2 = 0.28$]. The results are shown in Figure 4. It is interesting to note that even those individuals with no impairment displayed a mean score in the above average ($z > 1$) range for experiencing these symptoms [15].

Spectral power

Spectral power of QEEG activity was computed for each individual and analysed as a function of the degree of neuropsychological impairment. In order to determine general trends within the data, all the spectral power for each frequency band was summed. Results of these analyses revealed that global alpha power was significantly different between groups [$F_{(2,23)} = 3.69$, $p = 0.042$, eta$^2 = 0.26$].

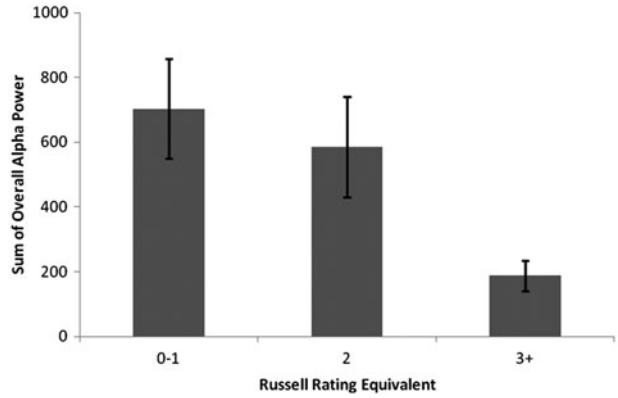

Figure 5. Means and standard deviations for the sums of the global alpha power from QEEG measurements as a function of the degrees of neuropsychological impairment.

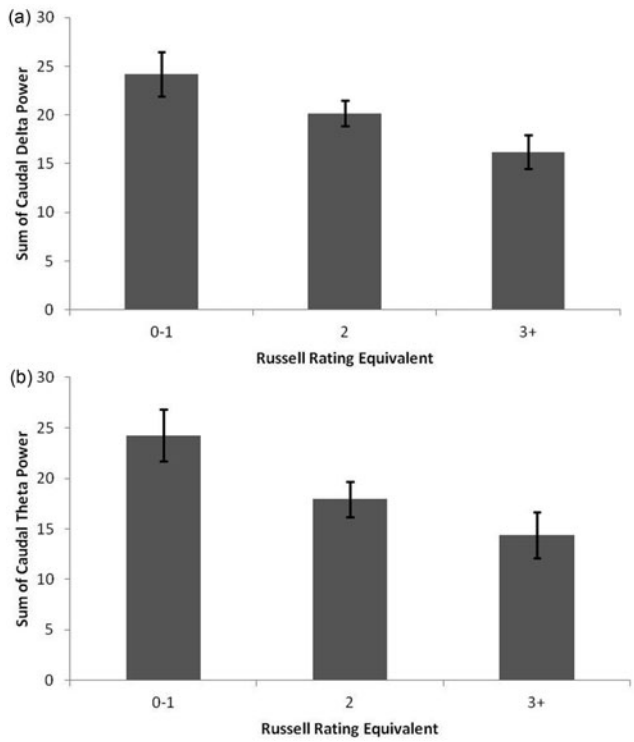

Figure 6. (a) Means and standard deviations for the sum power within the caudal cerebral regions as a function of the degree of neuropsychological impairment. (b) Means and standard deviations of the sum of power within the delta band for patients as a function of the degree of neuropsychological impairment.

Post-hoc analysis showed that the moderate–severe group exhibited significantly less global alpha power than the other groups (Figure 5). A non-parametric Kruskal-Wallis test confirmed the group differences ($\chi^2 = 6.47$, $p < 0.05$).

The results from comparing the spectral data with respect to rostral (frontal channels) and caudal (temporal, parietal, occipital regions with central regions excluded) regions were also revealing. Analyses (Figures 6(a) and (b)) revealed that the sums of the caudal delta [$F_{(2,23)} = 4.46$, $p = 0.024$, eta$^2 = 0.30$] and theta [$F_{(2,23)} = 4.93$, $p = 0.018$, eta$^2 = 0.32$] power were significantly reduced in individuals whose impairment was considered moderate–severe compared to those individuals who had no impairment.

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s-LORETA or source localization

s-LORETA analyses were completed where regions of interest (Brodmann areas) were selected individually and analysed for activation. The s-LORETA activation scores were summed based upon three regions (i.e. rostral, caudal and limbic), regardless of hemisphere. These regions were analysed with respect to the Halstead Impairment Index.

Analyses of variance revealed that activation of only the caudal hemisphere and limbic regions differed as a function of the groups' different level of impairment. Post-hoc analysis revealed that, for the most part, the group who was assessed to have a moderate–severe neuropsychological impairment showed significantly reduced activation compared to the group with no impairment [$F_{(2,23)} = 3.901$, $p = 0.036$, $\text{eta}^2 = 0.27$] as well as for limbic regions in the theta [$F_{(2,23)} = 7.676$, $p = 0.003$, $\text{eta}^2 = 0.42$] and low alpha [$F_{(2,23)} = 6.288$, $p = 0.007$, $\text{eta}^2 = 0.37$] and gamma [$F_{(2,23)} = 3.670$, $p = 0.043$, $\text{eta}^2 = 0.26$] bands. Within the limbic and caudal cortical regions the moderate–severe group showed significantly lower activation in the theta band compared to the other two groups (Figures 7(a) and (b)).

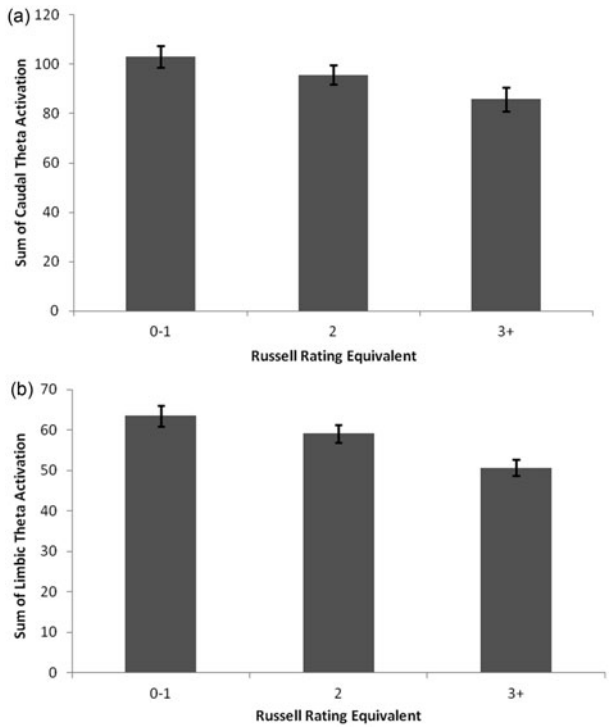

Figure 7. (a) Decreased caudal theta activation for individuals in the moderate–severe impairment group compared to individuals with no impairment. (b) Decreased limbic theta activation for individuals in the moderate–severe impairment group compared to individuals with no impairment and individuals with a mild impairment.

Microstate analysis

Microstate analysis was performed on the entire database of clients producing four microstates that explained 58% of the variance. Although the variance explained was considerably less than that typically reported in the literature [19], the global structure of the four microstates produced from this database were consistent with those previously identified (Figure 8). The red and blue reflect relatively similar magnitudes, but of opposite polarities.

Results of the analyses of the individual microstates for each client that were combined indicated a conspicuous relationship with the degree of neuropsychological impairment. The mean durations of the four microstates were negatively correlated with the impairment index (rho = -0.541, $p < 0.01$; $r = -0.573$, $p < 0.01$). This indicated that, as the neuropsychological impairment of the individual increased, the mean durations of the four microstates decreased (Figure 9).

Group differences were analysed for each individual microstate (class A–D). The durations of microstates A (rho = -0.462, $p < 0.05$; $r = -0.491$, $p < 0.05$), C (rho = -0.612, $p < 0.05$; $r = -0.475$, $p < 0.05$) and D (rho = -0.514, $p = 0.01$; $r = -0.536$, $p < 0.01$) were all significantly negatively correlated with the impairment index. Because age positively correlated with the impairment index (rho = 0.522, $p < 0.01$), age was also explored within this analysis. Results revealed that the class B microstate was negatively correlated with age (rho = -0.501, $p = 0.01$).

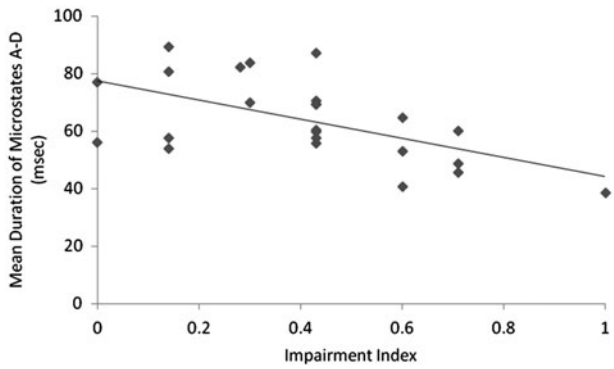

Figure 9. Correlation between the mean microstate durations and the individual's impairment index.

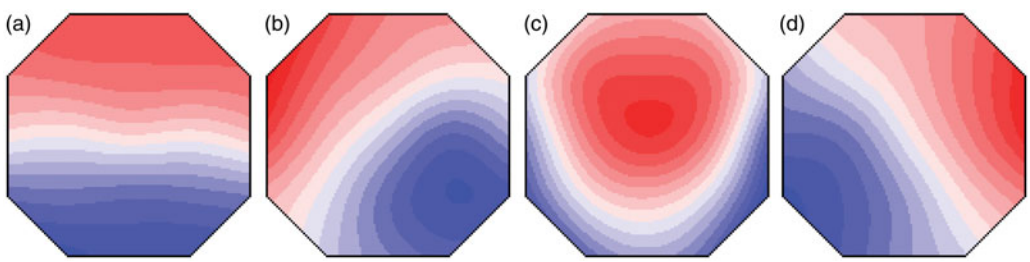

Figure 8. Average patterns for the four microstate maps obtained from the patient's global EEG activity.

Exploration of the literature showed that, as healthy individuals age, the asymmetrical microstates (classic classes A and B; from Koenig et al. [19]) decrease in duration, while the symmetrical microstates (classic classes C and D; from Koenig et al. [19]) increase. Although these results were not completely replicated it should be noted that the population being explored had sustained a significant brain injury. Perhaps these results indicate that the pattern of the class B microstate duration is the most stable over time, even after sustaining a significant injury.

Finally, global field power peaks significantly differed between groups of impairment for microstates A [$F_{(2,23)} = 4.48$, $p = 0.024$, $\text{eta}^2 = 0.30$] and D [$F_{(2,23)} = 4.18$, $p = 0.029$, $\text{eta}^2 = 0.29$]. Post-hoc analyses indicated that patients who displayed moderate–severe impairment displayed greater power than those with no impairments or mild impairments. The results are shown in Figure 10.

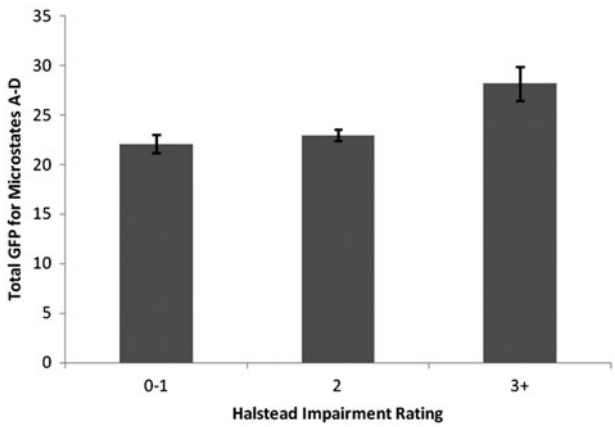

Figure 10. Total GFP for microstates A–D as a function of the different groups of neuropsychological impairments.

Qualitative differences in microstate configurations for impaired and non-impaired groups

In order to discern potential persistent differences in microstate configurations as well as the source locations for the configurations, microstates were obtained for the patients who displayed no impairment compared to the group who displayed moderate-to-severe neuropsychological impairment. The four microstates displayed for each group are shown in Figures 11 and 12. The configurations for the non-impaired group were similar to normal individuals. Three of the four configurations for the impaired group were similar. However, their microstate C displayed the source of the opposite polarity within the same (right) hemisphere.

Relationships between global power of each microstate and source localization activation

GFP or average global peak power can be considered a measure of the stability of the microstate. The primary sources of the correlations between each of the four microstates for the patients who displayed no neuropsychological impairment and for each of the four microstates for patients who displayed impairments consistent with mTBI are shown in Figures 13(a–d) and 14(a–d), respectively. In order to simplify and organize the large numbers of ROIs involved the data were grouped according to region. The solid rectangles indicate significant negative correlations with the average global field power (GFP) peaks, while dotted rectangles indicate positive correlations with average GFP peaks. The colours represent the frequency band, which were: green (delta), red (theta), blue (alpha), grey (beta) and black (gamma).

One parsimonious interpretation of the relationship between activation within the source localization (clusters of ROIs) and GFP is the following. For negative correlations, an increase in the stability of the peak power of the microstate

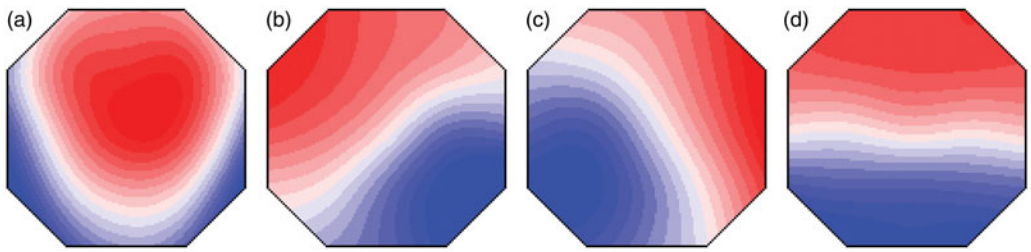

Figure 11. Microstate classes calculated for the group of individuals who were determined to have no impairment. The calculated microstates explained 60.8% of the variance.

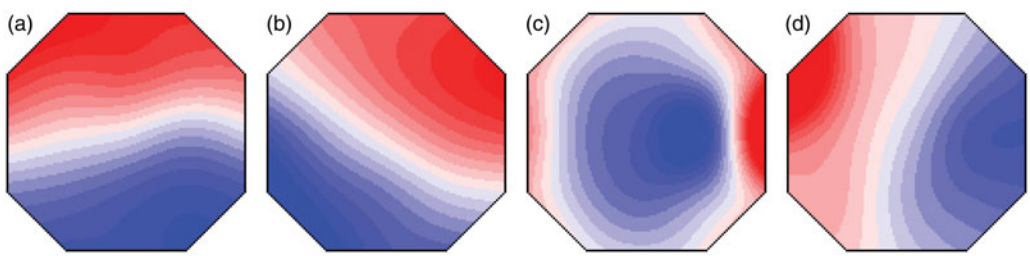

Figure 12. Microstate classes calculated for the group of individuals who were determined to have a moderate-to-severe impairment. The calculated microstates explained 52.1% of the variance.

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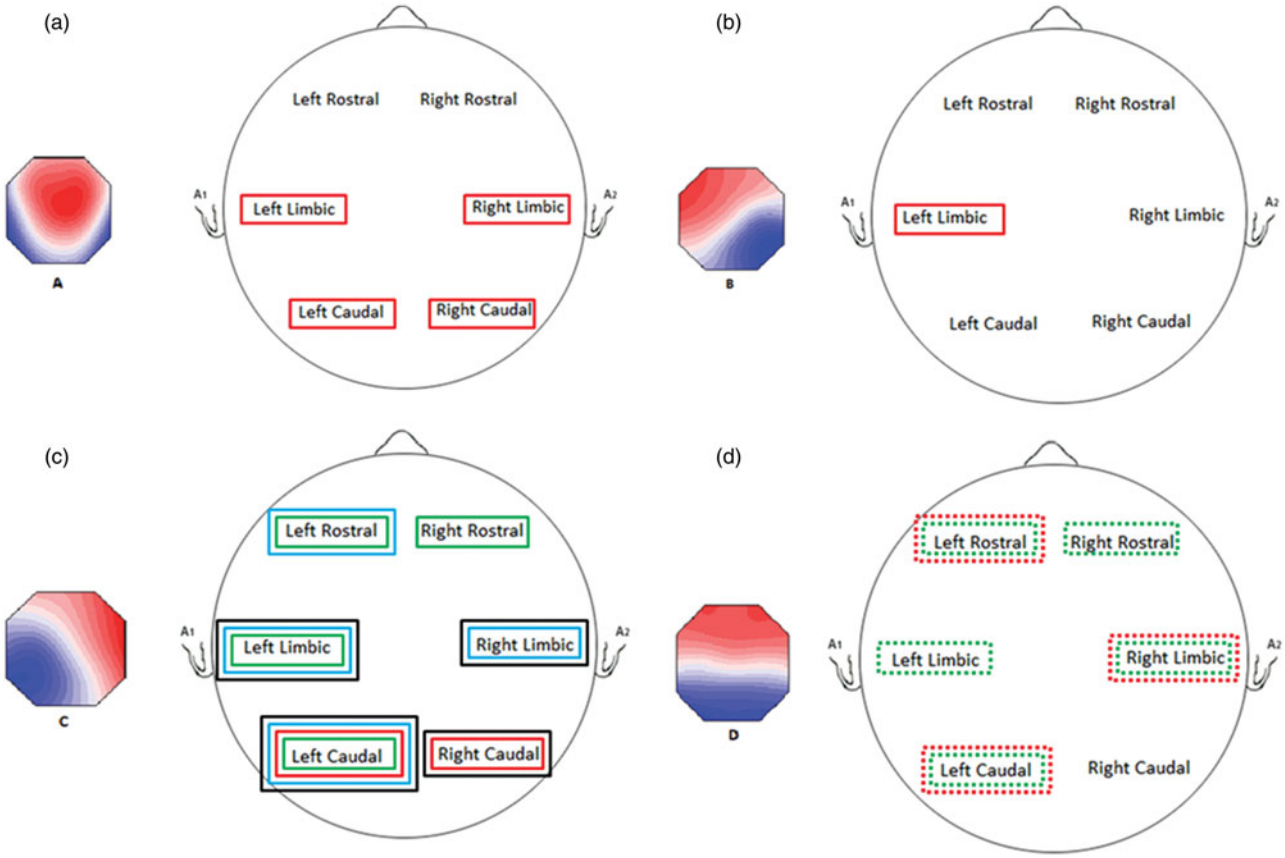

Figure 13. (a) Average global field power (GFP) peaks for individual's with no impairment for microstate A are negatively (solid line) correlated with source localization theta (red) activation in the left and right limbic regions and left and right caudal regions. (b) Average GFP peaks for individual's with no impairment for microstate B are negatively (solid line) correlated with source localization theta (red) activation in the left limbic region. (c) Average GFP peaks for individual's with no impairment for microstate C are negatively (solid line) correlated with source localization delta (green) activation in the left and right rostral region, left limbic region and left caudal region; theta (red) activation in the left and right caudal regions; alpha (blue) activation in the left rostral region, left and right limbic regions and left caudal region; gamma (black) activation in the left and right limbic regions and left and right caudal regions. (d) Average GFP peaks for individual's with no impairment for microstate D are positively (dotted line) correlated with source localization delta (green) activation in the left and right rostral region, right and left limbic regions and left caudal region; theta (red) activation in the left rostral region, right limbic region and left caudal region.

is associated with decrease activation of s-LORETA. Functionally this is similar to a diminished variability of standard deviation of scores for power across the different correlated ROIs. On the other hand positive correlations between GFP peaks and source localization indicate that, as the activation scores increase ('variability' increases) the stability of the peak power of that specific microstate decreases.

For the group who displayed no formal neuropsychological impairment the stability of microstate A was related to less activation in the limbic and caudal regions within both hemispheres. For microstates B, only the left limbic region contributed in this manner. The classic microstate C, which relates the right prefrontal coherence with the left caudal region, exhibited the typical rich association between less activation within the delta, theta, alpha and gamma bands within the left temporoparietal region and for all but theta activity in the left limbic structures. All other areas also contributed. On the other hand increased activation contributed to the GFP stability for microstate D.

The most conspicuous pattern for the group who displayed moderate-to-severe neuropsychological impairments typical of mild TBI was the relative absence of strong correlations between the clustered areas of interest and GFP stability. Except for the negative correlation between theta and gamma activity and the stability of microstate A within the rostral and caudal regions of the right hemisphere and the higher frequencies in the caudal regions of the left hemisphere there were no consistent associations.

Delay since the injury and source localization

The time between the mechanical impact and the neuropsychological assessment was not significantly correlated with the Halstead-Reitan Impairment Index; there was also no significant difference between the three groups for the latencies. However, the duration of time that had elapsed between the incidents and the QEEG measurements was revealing. As the time since the injury increased the source localizations for higher beta activity within the *left* temporal region (rho $= -0.56$, $p < 0.01$) and insular area (rho $= -0.45$, $p < 0.01$) decreased. A similar inverse relationship was noted in the left temporal lobe for beta 3 band.

Discussion

Although many patients who sustained mTBIs do not appear to display long-term dysfunctions or difficulties adapting, the scientific literature and clinical experience indicate there is a

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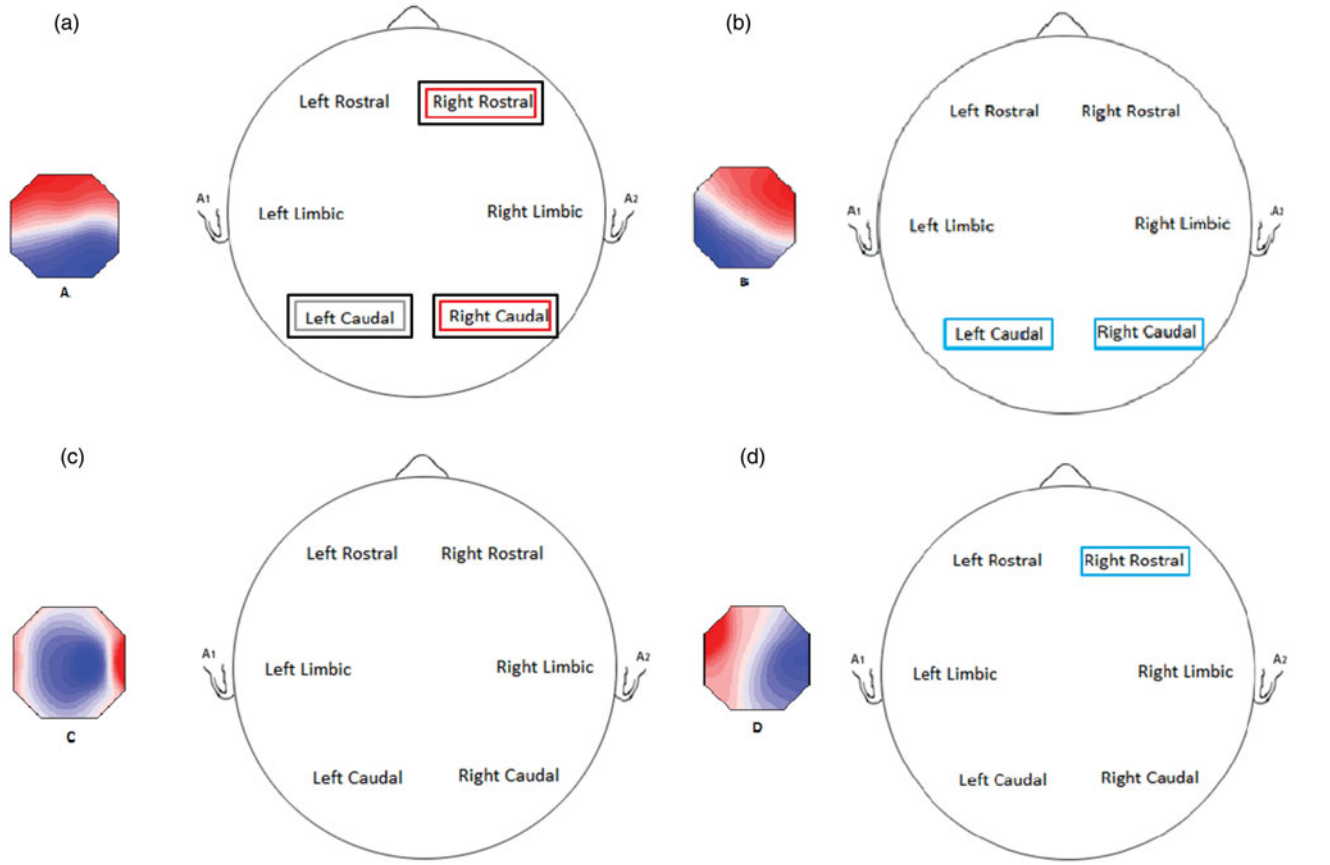

Figure 14. (a) Average global field power (GFP) peaks for individual's with a moderate-to-severe impairment for microstate A are negatively (solid line) correlated with source localization theta (red) activation in the right rostral region and right caudal; beta (grey) activation in the left caudal region; gamma (black) activation in the right rostral region and left and right caudal region. (b) Average GFP peaks for individual's with a moderate-to-severe impairment for microstate B are negatively (solid line) correlated with source localization alpha (blue) activation in the left and right caudal regions. (c) Average GFP peaks for individuals with a moderate-to-severe impairment for microstate C is not significantly correlated with any of the computed regions. (d) Average GFP peaks for individual's with a moderate-to-severe impairment for microstate D is significantly negatively (solid line) correlated with the alpha (blue) activation in the right rostral region.

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substantial sub-set of the population who do not easily adapt to the post-injury environment and exhibit the post-concussion syndrome or its many variants. Accurate and valid diagnosis of these patients is clearly important. However, what may be equally relevant is discerning the source localization and cerebral dynamic processes that may be contributing to their disability. More than one locus within the cerebral volume that exhibit mild dysfunctions and display the capacity to interact and transiently enhance each others' anomalies, like the summation and cancellation of multiple wave systems, could contribute to the often phasic incapacitation of patients for decades. Accurate isolation could be instrumental for designing treatments to at least partially compensate for the deficits. This study was designed to explore the utility of modern QEEG applications, particularly s-LORETA and microstates, to address these challenges.

It was reasoned that, to be clinically useful and practical, any patterns should be discernable within a small sample of patients as long as they exhibited the characteristics of the more general population. The empirical measurements from the patients assessed in this study were the first 26 from whom this study has extracted QEEG data of sufficient quality to apply to the various algorithms that define spectral profiles, s-LORETA and microstates. They were representative of the ~800 patients assessed thoroughly over the last 25 years without the benefit of QEEG technology. For example, the proportion of no impairment, mild and moderate-to-severe impairment were comparable. The primary differentiating psychometric indicators between levels of impairment, such as toe Graphaesthesia [10], the personality factor: liveliness [23], the MMPI scale for ruminative anxiety [12] and the elevated complex partial epileptic-like signs scores [13, 15] were similar to what has been measured in a previous assessment of the major population.

The general patterns that emerged from the present study were very clear and relevant to mTBI. First, for almost all measures, the classic EEG indicators (such as the sum of power within the alpha frequency band) of the patients within the group who displayed moderate-to-severe neuropsychological impairment (which constitutes the majority of patients who overlap with the mild TBI diagnosis in the authors' experience) differed from the group of patients who displayed no neuropsychological impairment. The mildly neuropsychologically impaired group occupied an intermediate level or did not differ significantly from the no-impairment group.

Like many other groups who have employed electroencephalographic measurements as collateral or correlative data for validating and facilitating interpretation of standardized scores from formal psychometric tests and neuropsychological test batteries, this study has observed the conspicuous

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rostral-caudal division in coherence of similar activity. This was evident even in the days of strip-chart recordings [24] and is now quantitatively clear with QEEG. However, unlike other approaches which show changes within frontal cortical parameters [3], the major differentiating indicator (power, i.e. $\mu V^2 Hz^{-1}$) found for sustained neuropsychological impairment years after the injury was lower frequency (delta and theta) power within the caudal hemisphere. Clustered frontal indicators did not differ between the impairment groups. This difference could suggest that the more immediate sequealae to mTBI are frontal disruptions involving organization of stimuli and behaviour, while residual effects years later involve the (caudal) regions involved with sensory and perceptual organization and processing.

The results from the two newer technologies applied in this study were quite revealing. The s-LORETA activation scores for theta activity within the caudal regions and the limbic areas were significantly less in the neuropsychologically impaired group compared to the patients whose assessments did not indicate impairment ~6 years after the TBI. The specificity of this frequency band is relevant because theta activity is well known to be associated with the proficiency and efficiency of memory [25, 26]. 'Memory', particularly for new information acquired since the injury, is one of the major complaints of these patients. Even at the most fundamental cellular level at which the variety of different durations of long-term potentiation (LTP) operates, the theta frequency range is critical for optimal consolidation of new experiences [27].

Perhaps the most useful tool for ascertaining the global and dynamic frequency-dependent differences in patients who display maintained neuropsychological impairment compared to those who do not was the microstates analyses. This technology may be one of the most comprehensive global vector measures available. Wackermann [28] has extracted single indicators to represent global activity, much like a single fractal number can be employed to describe a very complex and irregular geometric shape, that include three states: Sigma: a measure of global field strength in μV, Phi: a measure of global frequency of field changes in Hz, and Omega: a measure of spatial complexity (dimensionless). As superbly demonstrated by Koenig et al. [19], four microstates, that accommodate ~70% of the variance in QEEG activity as transient episodes of coherence over relatively large cerebral areas, are remarkably stable over people's life times. Their average durations, which range from 80–120 milliseconds, or on average would reflect the classical power peak of the cerebral output (10 Hz), are within the range of the percept. Assuming four fundamental states and an average of 100 milliseconds per state there would be 4^{10} combinations or ~1 million (1 MHz) variations per second. As suggested by Lehmann et al. [20] these microstates could be the 'building blocks', analogous to the base nucleotides for DNA sequences, for consciousness and information processing.

In the present study the microstates were representative of the general population. The group that displayed the most severe neuropsychological impairment exhibited significantly shorter average durations of microstates compared to the patients who did not display impairment. The approximate diminishment of duration for the impaired group was ~10–20 millisecond per microstate, which is within the range of the phase shift duration and recursive rostral-to-caudal cerebral fields associated with consciousness [29, 30]. Decreased durations of microstates have been reported for populations of patients exhibiting dementia [31] and within groups of schizophrenics [32]. Enhanced dementia-like symptoms and schizotypal behaviours, often indirectly reflected in increased incidence of complex partial epileptic-like syndromes, are common correlates of patients who display protracted difficulties subsequent to closed head injuries and mTBI [15]. The latter 'schizotypal' symptoms include persistent sensed presences, sudden shifts in states of consciousness and experiences of mystical states; they also have more direct neuroscientific explanations [33].

The results from calculation of microstates for the non-impaired and most neuropsychologically impaired groups were both confirming and revealing. The spatial configurations of the patients who were not impaired displayed the classic four shapes that are reported for normal individuals, including the non-patient population. The configurations for the group displaying neuropsychological impairments were anomalous, particularly one state, that showed both polarities in the same hemisphere. Such peculiarities have been shown in a single exceptional case where a right parietotemporal anomaly, likely from early childhood, was sufficient to be discerned as perfusion (SPECT) uptake anomalies as well [34]. The remarkable diminishment of correlations between the source location activation scores and the global power measurements for the impaired group in this study, if interpreted simplistically, would suggest these patients are impaired because of a dissociation or disconnection between coherence localization activity and the integration of microstates with which consciousness, the sense of now and information processing are associated.

From this approach the most effective treatments of mTBI must accommodate the physical, physicochemical and electromagnetic substrates to the symptoms. There are a myriad of mechanisms that have been individually pursued. They include accumulations of amyloid precursor protein, amyloid-beta peptide, neurofibrillary tangles and hyperphosporhylated tau (a microtubule associated protein), an enhanced disequilibrium of intracellular calcium [14] as well as multiple biomarkers that include S100B calcium-binding proteins, neuron-specific enolase and activated calpain/caspase [35]. Neurofibrillary tangles and amyloid-beta pathology occur in approximately one-third of patients who sustained a single TBI 1–47 years later [36]. However, the primarily histopathological correlate of mTBI in rodents that would not be easily discernable with the contemporary resolution of MRI are the scattered distributions of conspicuous shrunken, darkly stained neuronal soma that appear below the impact site of the mechanical force [37]. These cells remain there for months after the injury (rather than fragmenting) and are correlated with the severity of structure-specific behaviours [38]. The numbers of these dark stained neuronal somas below the impact site and at countercoup areas can be reduced by continuous post-impact exposure to weak, physiologically-patterned magnetic fields that contain components known to enhance long-term potentiation [39].

Employment of quantitative EEG measurements and extended algorithms to discern if patients reporting difficulties following mTBI are displaying neurocerebral anomalies in addition to those inferred from full neuropsychological assessments could be very useful for designing individual-based treatments. Although pharmacological approaches can be useful, they are often diffuse and not localized. Recent technology that employs computer-generated signals and engineering strategies to apply regional, physiologically-patterned, weak magnetic fields might be one solution to help these patients with apparently intractable dysfunctions to partially adapt [40]. Very weak magnetic fields rotating around the skull, with specific rates of change in angular velocity producing marked enhancements of gamma activity over the frontal and occipital regions when the average field velocity is $\sim$4–5 m s^{-1} or $\sim$7–8 Hz. This resonant frequency is also the solution [41] based upon cortical grey matter inductance (permeability) and capacitance (permittivity). Animal studies have found that brief, daily application of a patterned magnetic field to rats with brain injury resulted in persistent normalization of their behaviours [42]. One recent animal study [43] demonstrated that daily exposure to typical-intensity cell phone frequencies reduced the incidence of amyloid markers. Considering the increased proportion of patients who have sustained a closed head injury and earlier onset of dementia, these treatments may be relevant. There is now clear evidence of a biophysical linkage between EEG coherence and structural (MRI) measurements for patients who had sustained a TBI [44]. By knowing where within cerebral space and which frequency bands are most anomalous, custom-designed and compensatory magnetic fields could be applied.

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Declaration of interest

The authors report no conflict of interests. The authors alone are responsible for the content and writing of the paper.

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